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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,454	07/16/2003	Cheryl Fitzer-Attas	20555/1203432-US1	7700

7278 7590 12/28/2006

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EXAMINER	
STANDLEY, STEVEN H	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/619,454	FITZER-ATTAS ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *1-36,47 and 49-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-46 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II (claims 37-56) in the reply filed on 9/22/06 is acknowledged. The examiner also required an election of species but mistakenly included a claim generic to the species listed, which was "T-cell responses" of claim 46. Applicant elected claim 46, which is readable upon all the species recited in the species election. Therefore, the examiner required a further election of species among the remaining species claims (47-56), which was presented by phone to Mitchell Bernstein on the 14th of December 2006. Mr. Bernstein elected the species of claim 48, cytotoxicity. Claims 37-46, and 48 are now under examination.

Priority

2. Applicant has priority to provisional application 60/396,245, filed 7/17/02.

Information Disclosure Statement

3. The IDS filed 12/06 has been considered by the examiner.

Specification

4. The specification should be reviewed for improper recitation of hyperlinks. All such recitations should be deleted or amended such that the hyperlinks are rendered inactive. See MPEP § 608.01.

Claim Objections

5. Claim 42 is objected to because of the following informalities: line 2 of claim 42 reads, "wherein the based on the HLA," which is a grammatical error. Appropriate correction is required.

6. Claim 38 is objected to because of the following informalities: In step e line 3 from the top, delete "immune responses" because it is redundant. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 37-46, and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for selecting a peptide using the HLA Peptide Binding Predictions program on the Bioinformatics and Molecular Analysis Section website (//bimas.dcrt.nih.gov/molbio/hla_bind/) to identify sequences that probably bind to different haplotypes and then testing the binding of those sequences to different haplotypes in vitro, does not reasonably provide enablement for 'determining T-cell epitopes', 'predicting the reaction of an individual to a vaccine,' or 'a method of matching a vaccine.' Further, there is no nexus between scoring a peptide from A-beta as greater or less than "a

preselected value" and matching a vaccine, or predicting a reaction or even a method of determining T-cell epitopes. The method further depends The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of 'determining T-cell epitopes,' and 'a method of predicting the reaction of an individual to a vaccine,' and a method of matching a vaccine comprising a-beta to an individual.' However, all the specification teaches is use of a well-known website program for estimating the binding of to HLA class I molecules and subsequent testing of the predicted binding in vitro. The invention is complex because it attempts to apply an undisclosed "preselected value" for comparison as a means of determining 'T-Cell epitopes,' or 'predicting the reaction of an individual to a vaccine,' or 'matching a vaccine to an individual,' which are extremely complex and unpredictable things to do.

The state of the art is mixed. While it is well-known that one can predict the binding of peptides to MHC-I and MHC-II (see Parker et al, 1994, from Applicant's IDS' also See Mallios, 1999), it is not known that binding affinity of peptides is linked to cytotoxicity (let alone, the reaction of an individual to a vaccine, or matching an individual), and further there is no known "preselected value" that represents a threshold for determining cytotoxicity, or that determines the reaction of a patient, or that determines a match of an individual to a vaccine. Furthermore, the state of the art with regard to predicting the reaction to a vaccine, or reducing the autoimmunity to a vaccine (as described in the specification), is unpredictable and practically non-existent. For instance, Descotes et al (2002) disclose that "The mechanisms of these adverse reactions [in reference to allergy and autoimmunity in vaccines] are ill-elucidated, if at all. No animal models have been adequately standardized and validated to predict the risk of allergy and autoimmunity associated with vaccines [Abstract]." Thus, the art says predicting autoimmunity cannot be done.

There are no examples or guidance as to what a 'preselected value' is, what matching a vaccine constitutes, or how comparing the numeric output from the website calculation to a preselected value informs one of the reaction to a vaccine. There are no teachings as to how to match a vaccine to a patient based on the patient's HLA haplotype, no evidenciary showing that a screened peptide does match a patient for a vaccine, or deterimine the reaction to a vaccine, or even "determine T-cell epitopes."

The quantity of experimentation necessary to determine the reaction of a patient to a vaccine, or to match a patient to a vaccine by HLA haplotype would be, in effect, performing clinical trials with the peptide since the mechanisms of

autoimmunity are not known and the relationship between optimizing a peptide with a website program and the effect on a patient or the match between a patient is unknown and untaught in the specification.

Given the complex nature of the invention, the unpredictability and contrasting teachings in the art, the lack of guidance or example in the specification, and the quantity of experimentation necessary to successfully conclude such a method, one skilled in the art could not use the invention without undue experimentation.

8. Claims 37-46, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The invention recites comparing results to a "preselected value," however no such value is disclosed in the specification, nor is it disclosed how that "preselected value" determines t-cell epitopes or predicts the reaction of an individual or matches a vaccine to a patient.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art

to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required, or in the instant case, the "preselected value" is required. See *Fiers* v. *Revel*, 25 USPQ2d 1601 at 1606 (CMC 1993) and *Amgen Inc.* v. *Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 37-46 and 48 are rejected. Claims 37, 38 and 42 recite the limitation "a preselected value" in the final step. There is insufficient antecedent basis for this limitation in the claim. There is no step before wherein a value is selected. Claims 39-41, 43-46, and 48 are rejected as they depend from claims that lack antecedent basis.

10. Claims 37-46, and 48 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite determining a

"binding value" for each amino acid. However, it is unclear what a "binding value" constitutes. For instance, is it a Kd, is it a Ka, is it a ratio of something? It is unclear.

11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Parker et al (1994; in Applicant's IDS).

Parker et al determine epitopes within many peptides (see table VII) which are 'homologues' of a-beta by determining a binding value of each amino acid (see table V), determining the resulting score (table VII), and comparing the resulting score to a preselected value (see 'experimental value' in Table VII) to predict the presence of binding epitopes or 'T-cell epitopes.'

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through

Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
12/17/06

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER